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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,143	05/22/2007	Barbara Jane Johnson	SPRUS63.001 APC	1825

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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
03/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/586,143	JOHNSON ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Restriction Requirement:

In response of 2 December 2008, Applicants canceled claims 1-29 and 34-39, rending the requirement for restriction moot.

Claims 30-33 are pending and under consideration in the instant application.

Objections

Claims:

Claim 30 is objected to as reciting "Cpn10" A protein should be identified by its full name the first time it is recited in the claims. It is suggested the claim be amended to recite "Chaperonin 10 (Cpn 10)…".

35 U.S.C. § 112, First Paragraph:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or **use** the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include,

but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims of the instant invention are drawn to an isolated molecular complex comprising a Toll-like receptor, Toll-like receptor agonist and Cpn10.

The specification teaches that Cpn10, Toll-like receptors and Toll-like receptor agonists form a molecular complex. FRET analysis suggests that there may be a direct interaction between Cpn10 and Toll-like receptor, or that at least they are in very close spatial proximity (within 1-10 nm of each other), in the presence of TLR ligand (e.g. LPS) [paragraph 0072 of PGPUB 20070275890, the PGPUB of the instant invention]. The specification teaches complexes comprising TLR2, LPS and Cpn10 and complexes comprising TLR4, lipoprotein and Cpn10. Thus, one of ordinary skill in the art could envision how to make such an isolated complex, for example, by combining all the recited elements. However, 35 U.S.C. 112, first paragraph also requires that the specification enable one of ordinary skill in the art to **use** the claimed invention. One of ordinary skill in the art would not be able to use the claimed invention without undue experimentation.

The specification teaches that the molecular complex comprising Cpn10, a Toll-like receptor, and a Toll-like receptor agonist may be used to produce, design or screen a Cpn10 agonist or antagonist [paragraph 0149 of PGPUB 20070275890, the PGPUB of the instant invention]. A candidate agonist may be identified by an ability to form a molecular complex with a Toll-like receptor and a Toll-like receptor agonist. However, the claims recite a complex comprising a Toll-like receptor, a Toll-like receptor agonist and Cpn10. Insufficient guidance is given as to how one may use the complex to identify candidate agonists utilizing the complex of the instant invention, as the teachings in the specification disclose that one would do so by using a complex comprising a Toll-like receptor and a Toll-like receptor agonist. These are not the components recited by the claims of the instant invention (which are directed to an

isolated molecular complex comprising Cpn10, a Toll-like receptor and a Toll-like receptor agonist). Thus, the specification does not teach how to utilize the complex of the claimed invention to identify a candidate agonist.

A candidate antagonist may be identified by an ability to prevent or disrupt formation of a molecular complex comprising Cpn10, a Toll-like receptor and a Toll-like receptor agonist [paragraphs 0151-0152]. With respect to identification of an antagonist, the specification does not teach how one is to detect disruption of formation of the complex. The specification teaches "The elucidation of the effect of Cpn10 upon Toll-like receptor signaling and immunomodulator secretion provides a new and unexpected opportunity whereby Cpn10 agonists and antagonists may be specifically designed or screened according to their effect upon Toll-like receptor signaling and immunomodulator secretion" [paragraph 0135].

Insufficient guidance is given to one of ordinary skill in the art would be to allow one to determine how to screen for agonists and antagonists by detecting their effect upon Toll-like receptor signaling and immunomodulator secretion utilizing an isolated complex; one of ordinary skill would recognize that the Toll-like receptor, being a membrane bound receptor, may not function as part of an isolated complex. Furthermore, the claimed complex is an isolated one; the specification provides no guidance as to how one is to detect Toll-like receptor signaling or immunomodulator secretion absent an intact cell comprising the recited complex.

Additionally, one of ordinary skill in the art would be unable to predict that all TLRs and their cognate agonists would be able to form isolated complexes with Cpn10. Huang et al. (2008. Oncogene 27:218-224) teach that 13 mammalian TLR analogs have been identified. Different TLRs exhibit specificity for pathogen-derived ligands TLRs 2, 3, 4, 5, 7 and 9 recognize bacterial lipoproteins, double-stranded RNA/poly (I:C), lipopolysaccharides, flagellin, single stranded RNA and CpG-containing DNA, respectively. The ligands for TLR 10, 12 and 13 remain unidentified. Applicants have not identified how these complexes are formed, and which structures must be present to enable formation of such complexes. Given the number of TLRs, and the diverse

nature of their cognate ligands, one would not predict that complexes between any TLR, other than those comprising TLR2 and TLR4, agonist and Cpn10 could be formed.

The working examples teach immunoprecipitation of Cpn10 with TLR4 in the presence of a ligand (Example 4), strong association of Cpn10 with TLR4 upon LPS stimulation and disclose that this complex localizes to lipid rafts in the cell membrane of the intact cell (Example 5). There are no examples, working or prophetic, that teach utilization of the isolated complex of the claimed invention to produce, design or screen a Cpn10 agonist or antagonist.

The teachings in the art do not overcome the deficiencies in the specification. Huang et al. (2008. Oncogene 27:218-224) teach that 13 mammalian TLR analogs have been identified. TLRs 1, 2, 4, 5, and 6 are expressed on the cell surface; TLRs 3,7,8,and 9 are found almost exclusively within endosomes (page 218, 2nd column, 2nd paragraph). One of ordinary skill in the art would predict that the functioning of the TLR receptors would be dependent on the precise localization in the cell, and that functioning of TLR2 and 4, recited in the claims of the instant invention, would require precise orientation within the cell membrane. Thus, one of ordinary skill would not predict that one could screen for agonists and antagonists of Cpn10 using the isolated complex as recited in the claims of the instant invention.

Due to the large quantity of experimentation necessary to determine how to use the isolated complex of the instant invention, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing that TLR2 and TLR4 are membrane bound receptors, and the breadth of the claims which recite complexes comprising any TLR and any TLR receptor agonist, undue experimentation would be required of the skilled artisan to make and/or **use** the claimed invention.

Written Description

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph.

The claim is drawn to an isolated molecular complex comprising **any** Toll-like receptor, **any** Toll-like receptor agonist and Cpn10.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., an isolated molecular complex comprising **any** Toll-like receptor, **any** Toll-like receptor agonist.and Cpn10.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is identification of a class of receptors and agonists of said receptors. The claims do not identify which part of the receptor-agonist complex is responsible for formation of a molecular complex with Cpn10. There is no identification of any particular portion of the TLR or agonist structure that must be present so that the entire molecular complex may be formed utilizing any TLR and its any agonist.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation

of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

There are two species of the claimed genus disclosed that are within the scope of the claimed genus, *i.e.* an isolated molecular complex comprising TLR2, a lipopeptide and Cpn10 and an isolated molecular complex comprising TLR4, LPS and Cpn10. The disclosure of a small number of disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus.

However, the art (Huang et al, page 218, 2nd column, 2nd paragraph) describes at least 13 mammalian TLR analogs. Different TLRs exhibit specificity for different pathogen-derived ligands. TLRs 2, 3, 4, 5, 7 and 9 recognize bacterial lipoproteins, double-stranded RNA/poly (I:C), lipopolysaccharides, flagellin, single stranded RNA and CpG-containing DNA, respectively. The ligands for TLR 10, 12 and 13 remain unidentified. Takeda et al (2003. Ann Rev Immunol 21:335-76) present a table (Table 1) listing many TLR ligands of diverse chemical structure and origin.

It is thus clear that the claims of the instant invention encompass numerous isolated molecular complexes that are not further described.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is an isolated molecular complex comprising **any** Toll-like receptor, **any** Toll-like receptor agonist.and Cpn10. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas- Cath* at page 1116).

Therefore, only a molecular complex comprising TLR2, a lipopeptide and Cpn10 and a molecular complex comprising TLR4, LPS and Cpn10, but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Prior art made of record:

The following prior art is made of record and not relied upon is considered pertinent to applicant's disclosure.

Morton et al (WO 95/15338) teach Cpn10 acts as an immunosuppressive factor (page 5, lines 20-22) and may be used to treat autoimmune diseases (pages 21-23). Coates et al (WO 02/40038) teach that Cpn10 may be used to treat allergic conditions such as asthma, rhinitis/hay fever, eczema and anaphylaxis and acts to suppress pro-inflammatory over-reactivity (abstract). However, neither reference teaches an isolated molecular complex comprising a Toll-like receptor, a Toll-like receptor agonist and Cpn10.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. H. S./
Examiner, Art Unit 1647

/Manjunath N. Rao, /
Supervisory Patent Examiner, Art Unit 1647